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## Are Molecular Vibration Patterns of Cell Structural Elements Used for Intracellular Signalling?

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### Abstract:

#### Background:

To date the manner in which information reaches the nucleus on that part within the three-dimensional structure where specific restorative processes of structural components of the cell are required is unknown. The soluble signalling molecules generated in the course of destructive and restorative processes communicate only as needed.

#### Hypothesis:

All molecules show temperature-dependent molecular vibration creating a radiation in the infrared region. Each molecule species has in its turn a specific frequency pattern under given specific conditions. Changes in their structural composition result in modified frequency patterns of the molecules in question. The main structural elements of the cell membrane, of the endoplasmic reticulum, of the Golgi apparatus, and of the different microsomes representing the great variety of polar lipids show characteristic frequency patterns with peaks in the region characterised by low water absorption. These structural elements are very dynamic, mainly caused by the creation of signal molecules and transport containers. By means of the characteristic radiation, the area where repair or substitution services are needed could be identified; this spatial information complements the signalling of the soluble signal molecules. Based on their resonance properties receptors located on the outer leaflet of the nuclear envelope should be able to read typical frequencies and pass them into the nucleus. Clearly this physical signalling must be blocked by the cell membrane to obviate the flow of information into adjacent cells.

#### Conclusion:

If the hypothesis can be proved experimentally, it should be possible to identify and verify characteristic infrared frequency patterns. The application of these signal frequencies onto cells would open entirely new possibilities in medicine and all biological disciplines specifically to influence cell growth and metabolism. Similar to this intracellular system, an extracellular signalling system with many new therapeutic options has to be discussed.

**Keywords:** Infrared radiation, intracellular signalling, molecular vibration, membrane, nuclear envelope, polar lipids.

## INTRODUCTION

In recent decades a remarkable gain in the knowledge of structures and functional processes in living cells has been achieved. The structure of the cell membrane, of the endoplasmic reticulum (ER), the nucleus membrane, the Golgi apparatus, the mitochondria, the cytoskeleton, and other structural components have already been explained in detail [1 - 4]. The basic elements of the cell membrane and the majority of the structural elements are lipid bilayers consisting of numerous polar lipids, cholesterol, and specific proteins, many of which are organized in specific substructures, the rafts [3, 5, 6]. The main paths of the chemical signal transduction from reception at the outer cell membrane to the nucleus or the organelles and to the network of intracellular signal transduction pathways have been for the most part

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identified [7]. The transport of various components through the membrane and the generation of signal substances in the membranes are also well studied. The generation of transport vesicles originating from the Golgi or the ER and the actively directed transport by means of microtubules and motor proteins has been elucidated [8, 9] as well. The processes in the cell nucleus, *i.e.*, transcription, translation, repair and monitoring processes and a plentitude of aspects of posttranslation and of all the aspects of the processes of synthesis in the ribosomes have been studied extensively. The entire logistics of the efferent transport of biomolecules is quite understandable although not completely explained in detail. Presently under discussion is the idea that the transport processes in the microtubules by motor proteins are realized or at least controlled by means of electromagnetic energy [10 - 12]. The energy required is provided in the form of high-energy phosphate compounds in the mitochondria. The destinations of transported substances are in part defined in the components transported [13].

A portion of the afferent information flow within this highly complex process is still not understood. Indeed the structural components exhibit high plasticity and are permanently restored; relevant structural components of the membrane such as phospholipids or shingolipids are converted into soluble signal substances by specific enzymes. Thus, they have to be substituted, or an ER or Golgi fraction needs to be replaced because it has been used for transporting tasks. The required polar lipids are in most cases synthesized at very different places in the ER and have to be transported *via* cytoplasm by the Golgi and intramembraneously by cassette proteins; accordingly the enzyme systems required have to be activated. The information dealing with the requirement of substitution is mainly transferred by the soluble products of the cleavage of the membrane lipids and their derivatives. Candidate for this signaling are eicosanoids, including leukothriens, prostaglandines, thromboxanes, lipoxins and lysophospholipids, lysosphingolipids and others. However, the exact area in these three-dimensional spaces where substitution or restoration needs to be accomplished cannot be reported by these signal substances. The "lateral self-organization" in the membranes is no explanation for many of the restorative processes. Most probably this is controlled by the nucleus and possibly by the mitochondria. Information on particular changes of the structural components from different parts of the cell has to be delivered to the nucleus. What options are available to the cell for this purpose? It seems plausible that, in addition to the chemical signalling, a signal system based on a physical principle exists capable of controlling the spatial structures.

## HYPOTHESIS

All molecules show oscillatory behavior above absolute zero, *i.e.* normal molecular vibration, whose intensity is dependent on temperature. At the temperature of living eukaryotic animal cells of about 310- 313°K the intensity of this vibration is remarkable. The energy for the vibration being provided by the metabolic processes of the cells as reaction enthalpy. The frequencies of the individual oscillating molecular groups in a given molecule depend on the type of the atoms bound. The nature and polarity of the bonds, and secondarily the adjacent molecules and the phase structure. The frequency pattern is typical of the substance under the prevailing condition. The macromolecules contain few functioning groups which polarize the molecule. These groups are dominant in the vibration spectrum while the mass of the vibration frequencies generated by the carbon hydrogen bonds of the macromolecule results in broad, undifferentiated frequency bands. The molecular vibration generates an equivalent infrared radiation (IR) [14]. For single molecules and molecule groups, there are characteristic frequency patterns with defined peaks already used in modern chemical analysis. With the help of infrared and Raman spectroscopy, the characteristic spectra of molecular vibrations of many biomolecules have been determined for various tissues and recorded in comprehensive files [15, 16]. The peaks are in the range of 400 to 3000 $\text{cm}^{-1}$  ( $10^{11}$  - $10^{14}$  Hz). Molecules with strongly polarized groups usually exhibit pronounced maxima. Many of the vibration peaks of polar lipids, particularly of phospholipids in membranes, are found in the range of 1000-1200 $\text{cm}^{-1}$  where water absorption is low [15, 16]. The amount of a molecule's or a molecular group's radiated energy is very small. The totality of the frequency pattern forms an exact image in terms of chemical composition and physical state at a location such as the rafts. It would be extremely difficult to control all of them since each type of molecule has its own vibration profile as modified by its specific structural organization. However, changes of the membrane structural elements caused by chemical reactions are characterized by activation of a great number of molecules which signal chemical and organizational deviations. This does not only result in changed radiation patterns but also in an increase in the energy emitted. This could be important in selecting relevant information at the basic level. As most of the molecules around the structural elements are water, with absorption in the range of 1300-1900  $\text{cm}^{-1}$ , these sequences should not be preferred. Extraordinary requirements on the receptor would be needed concerning the selection of the information provided by the electromagnetic signals. Identification could be based on the resonance principle for specific peaks. This information should be processed for transfer into the nucleus. If the

outer side of the membrane of the cell nucleus or the connected ER would be able to read this information, a variety of further steps could be envisaged, *i.e.*, induction of directional transport tasks or signal transduction through the nuclear envelope and the inducing of transcription, translation, and initiation of the entire efferent supply chain to the location of necessary action and the restoration of the original state. Essential for this process would be:

- Structurally and functionally relevant information reaches the nucleus' membrane,
- Specific receptors able to process the signals are present on the outside of the nuclear envelope or of the associated ER-membrane, and
- The information remains exclusively within the specific cell and is not transferred to the adjacent cells.

To 1: The penetration depth of photons in the infrared region in animal tissue is a few millimeters, depending on the wavelength [17, 18]; IR frequencies with wavelengths of 650-1450nm show the best penetration for reasons of lowest water absorption [19]. Most cells have a diameter in the range of a few  $\mu\text{m}$ . The conductive structures of the intracellular membranes could be important here. The polar membrane layer of the ER facing the cytoplasm produces a small number of layers of quasi-crystalline, ordered water molecules. This phenomenon could be of additional relevance. The intracellular distances thus seem bridged in this fashion.

To 2: The nuclear envelope consists of the outer and inner membrane sheet and the underlying lamina [20 - 23]. A substantial portion of the outer layer of the membrane consists of polar lipids, wherein a large part of the more than 1000 different molecular species of the cell lipidomics can be found [1 - 4]. More than 70% are specific proteins closely associated in part with the lipids and form complex pore structures for the transport of biomolecules through the membrane. Specific proteins provide the link between the interior of the nucleus, including the genome, the various layers of nuclear envelope and the cytoskeleton and microtubules [24 - 27]. Proteins serve to anchor the nucleus in the cell. Similar to the outer cell membrane, assembled in the rafts there are complex structural elements of different lipid and protein species showing striking phase changes under specific conditions. The single lipids in the complex raft structure, as well as protein structures, stand to question as candidates for receptor functions. The transduction of electromagnetic signals received in the nucleus is still not understood. Signaling lipid molecules could be important here [7, 28, 29].

To 3: Electromagnetic waves are strongly attenuated when they impinge on layers with a structure of cell membranes (successive polar hydrophilic layer, hydrophobic, quasi-crystalline layer with long carbohydrate chains, hydrophilic layer) with an electric charge; this means the photons scarcely leave the cell. Additionally, they would be strongly weakened during penetration into a neighboring cell. Hence, they would have no adverse effect on neighboring cells. The influence at the cellular metabolism of electromagnetic energy externally applied is the subject of numerous studies. It has been demonstrated that frequencies of 30-300GHz induce numerous membranous and DNA changes and finally apoptosis [30]. Eukaryotic cells generate a relatively wide electromagnetic frequency spectrum 1-500MHz [10]. Intracellular effects, however, have hardly been studied in terms of their importance for afferent signalling in the cell.

## CONCLUSION

The hypothesis as stated must be proved experimentally, taking into account different cell cultures, isolated artificial and living cell membranes, isolated cell nuclei, and a great variety of IR applications. Based on the known vibration patterns of single polar lipids, cholesterol, and specific proteins, the changes of those patterns in the complex structures of the rafts have to be determined. The change of electromagnetic signal patterns induced by the action of phospholipases and spingomyolinsases onto membranes transforming structural elements into soluble signalling molecules should be recorded.

Experimentally generated frequency patterns detected as candidates should be applied intracellularly to isolated cells and to isolated nuclear envelopes to trigger typical responses. A noteworthy challenge would be in identifying the receptor system.

If the hypothesis can be proved, new knowledge of the function of living cells could be gained and many completely new possibilities of action within cells would arise, which could be important in medicine and, more generally, in the many branches of biological science. A similar extracellular physical signalling system can be discussed with numerous therapeutic options.

## CONFLICT OF INTEREST

The author confirms that this article content has no conflict of interest.

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## REFERENCES

- [1] van Meer, G.; Voelker, D.R.; Feigenson, G.W. Membrane lipids: where they are and how they behave. *Nat. Rev. Mol. Cell Biol.*, **2008**, *9*(2), 112-124.  
[<http://dx.doi.org/10.1038/nrm2330>] [PMID: 18216768]
- [2] van Meer, G. Cellular lipidomics. *EMBO J.*, **2005**, *24*(18), 3159-3165.  
[<http://dx.doi.org/10.1038/sj.emboj.7600798>] [PMID: 16138081]
- [3] Simons, K.; Sampaio, J.L. Membrane organization and lipid rafts. *Cold Spring Harb. Perspect. Biol.*, **2011**, *3*(10), a004697.  
[<http://dx.doi.org/10.1101/cshperspect.a004697>] [PMID: 21628426]
- [4] English, A.R.; Voeltz, G.K. Endoplasmic reticulum structure and interconnections with other organelles. *Cold Spring Harb. Perspect. Biol.*, **2013**, *5*(4), a013227.  
[<http://dx.doi.org/10.1101/cshperspect.a013227>] [PMID: 23545422]
- [5] Amazon, J.J.; Feigenson, G.W. Lattice simulations of phase morphology on lipid bilayers: renormalization, membrane shape, and electrostatic dipole interactions. *Phys. Rev. E Stat. Nonlin. Soft Matter Phys.*, **2014**, *89*(2), 022702.  
[<http://dx.doi.org/10.1103/PhysRevE.89.022702>] [PMID: 25353504]
- [6] García-Sáez, A.J.; Schwille, P. Stability of lipid domains. *FEBS Lett.*, **2010**, *584*(9), 1653-1658.  
[<http://dx.doi.org/10.1016/j.febslet.2009.12.036>] [PMID: 20036662]
- [7] Serhan, C.N.; Haegström, J.Z.; Leslie, C.C. Lipid mediator networks in cell signaling: update and impact of cytokines. *FASEB J.*, **1996**, *10*(10), 1147-1158.  
[PMID: 8751717]
- [8] Pavin, N.; Tolić-Nørrelykke, I.M. Dynein, microtubule and cargo: a ménage à trois. *Biochem. Soc. Trans.*, **2013**, *41*(6), 1731-1735.  
[<http://dx.doi.org/10.1042/BST20130235>] [PMID: 24256283]
- [9] Franker, M.A.; Hoogenraad, C.C. Microtubule-based transport - basic mechanisms, traffic rules and role in neurological pathogenesis. *J. Cell Sci.*, **2013**, *126*(Pt 11), 2319-2329.  
[<http://dx.doi.org/10.1242/jcs.115030>] [PMID: 23729742]
- [10] Pokorný, J.; Pokorný, J.; Kobilková, J. Postulates on electromagnetic activity in biological systems and cancer. *Integr. Biol. (Camb)*, **2013**, *5*(12), 1439-1446.  
[<http://dx.doi.org/10.1039/c3ib40166a>] [PMID: 24166132]
- [11] Cifra, M.; Pokorný, J.; Havelka, D.; Kucera, O. Electric field generated by axial longitudinal vibration modes of microtubule. *Biosystems*, **2010**, *100*(2), 122-131.  
[<http://dx.doi.org/10.1016/j.biosystems.2010.02.007>] [PMID: 20178826]
- [12] Havelka, D.; Cifra, M.; Kučera, O.; Pokorný, J.; Vrba, J. High-frequency electric field and radiation characteristics of cellular microtubule network. *J. Theor. Biol.*, **2011**, *286*(1), 31-40.  
[<http://dx.doi.org/10.1016/j.jtbi.2011.07.007>] [PMID: 21782830]
- [13] Blobel, G. Intracellular protein topogenesis. *Proc. Natl. Acad. Sci. USA*, **1980**, *77*(3), 1496-1500.  
[<http://dx.doi.org/10.1073/pnas.77.3.1496>] [PMID: 6929499]
- [14] Atkins, W.; de Paula, J. *Physikalische Chemie*, 5<sup>th</sup> ed.; Wiley-VCH: Germany, **2002**, pp. 467-500.
- [15] Zimmerer, C.; Steiner, G. Infrared and Raman Spectra. In: *Landolt Börnstein*; Arndt, K.F.; Lechner, M.D., Eds.; Springer Berlin: Heidelberg, **2013**; 6, pp. 253-443.
- [16] Mosaghi, Z.; Rehman, S.; Rehman, I.U. Fourier Transform Infrared (FTIR) spectroscopy of biological tissues. *Appl. Spectrosc. Rev.*, **2008**, *43*, 134-179.  
[<http://dx.doi.org/10.1080/05704920701829043>]
- [17] Neumeister, V.; Scheibe, M.; Lattke, P.; Jaross, W. Determination of the cholesterol-collagen ratio of arterial atherosclerotic plaques using near infrared spectroscopy as a possible measure of plaque stability. *Atherosclerosis*, **2002**, *165*(2), 251-257.  
[[http://dx.doi.org/10.1016/S0021-9150\(02\)00279-4](http://dx.doi.org/10.1016/S0021-9150(02)00279-4)] [PMID: 12417275]
- [18] Jaross, W.; Neumeister, V.; Lattke, P.; Schuh, D. Determination of cholesterol in atherosclerotic plaques using near infrared diffuse reflection spectroscopy. *Atherosclerosis*, **1999**, *147*(2), 327-337.  
[[http://dx.doi.org/10.1016/S0021-9150\(99\)00203-8](http://dx.doi.org/10.1016/S0021-9150(99)00203-8)] [PMID: 10559519]

- [19] Pansare, V.; Hejazi, S.; Faenza, W.; Prud'homme, R.K. Review of long-wavelength optical and NIR aging materials: Contrast agents, fluorophores and multifunctional nano carriers. *Chem. Mater.*, **2012**, *24*(5), 812-827. [<http://dx.doi.org/10.1021/cm2028367>] [PMID: 22919122]
- [20] Burke, B.; Stewart, C.L. Functional architecture of the cell's nucleus in development, aging, and disease. *Curr. Top. Dev. Biol.*, **2014**, *109*, 1-52. [<http://dx.doi.org/10.1016/B978-0-12-397920-9.00006-8>] [PMID: 24947235]
- [21] Cau, P.; Navarro, C.; Harhour, K.; Roll, P.; Sigaudy, S.; Kaspi, E.; Perrin, S.; De Sandre-Giovannoli, A.; Lévy, N. Nuclear matrix, nuclear envelope and premature aging syndromes in a translational research perspective. *Semin. Cell Dev. Biol.*, **2014**, *4*, 00058-00065. [<http://dx.doi.org/10.1016/j.semcdb.2014.03.022>]
- [22] Cain, N.E.; Starr, D.A. SUN proteins and nuclear envelope spacing. *Nucleus*, **2015**, *6*(1), 2-7. [<http://dx.doi.org/10.4161/19491034.2014.990857>] [PMID: 25425085]
- [23] Guo, T.; Fang, Y. Functional organization and dynamics of the cell nucleus. *Front. Plant Sci.*, **2014**, *5*, 378. [<http://dx.doi.org/10.3389/fpls.2014.00378>] [PMID: 25161658]
- [24] Tapley, E.C.; Starr, D.A. Connecting the nucleus to the cytoskeleton by SUN-KASH bridges across the nuclear envelope. *Curr. Opin. Cell Biol.*, **2013**, *25*(1), 57-62. [<http://dx.doi.org/10.1016/j.ceb.2012.10.014>] [PMID: 23149102]
- [25] Rothballer, A.; Kutay, U. The diverse functional LINC's of the nuclear envelope to the cytoskeleton and chromatin. *Chromosoma*, **2013**, *122*(5), 415-429. [<http://dx.doi.org/10.1007/s00412-013-0417-x>] [PMID: 23736899]
- [26] Burns, L.T.; Wente, S.R. Trafficking to uncharted territory of the nuclear envelope. *Curr. Opin. Cell Biol.*, **2012**, *24*(3), 341-349. [<http://dx.doi.org/10.1016/j.ceb.2012.01.009>] [PMID: 22326668]
- [27] Rothballer, A.; Schwartz, T.U.; Kutay, U. LINCing complex functions at the nuclear envelope: what the molecular architecture of the LINC complex can reveal about its function. *Nucleus*, **2013**, *4*(1), 29-36. [<http://dx.doi.org/10.4161/nucl.23387>] [PMID: 23324460]
- [28] Faenza, I.; Fiume, R.; Piazzini, M.; Colantoni, A.; Cocco, L. Nuclear inositide specific phospholipase C signalling - interactions and activity. *FEBS J.*, **2013**, *280*(24), 6311-6321. [<http://dx.doi.org/10.1111/febs.12450>] [PMID: 23890371]
- [29] Farooqui, A.A.; Ong, W.Y.; Farooqui, T. Lipid mediators in the nucleus: Their potential contribution to Alzheimer's disease. *Biochim. Biophys. Acta.*, **2010**, *1801*, 906-916. [<http://dx.doi.org/10.1016/j.bbalip.2010.02.002>]
- [30] Wu, G.; Chen, X.; Peng, J.; Cai, Q.; Ye, J.; Xu, H.; Zheng, C.; Li, X.; Ye, H.; Liu, X. Millimeter wave treatment induces apoptosis via activation of the mitochondrial-dependent pathway in human osteosarcoma cells. *Int. J. Oncol.*, **2012**, *40*(5), 1543-1552. [<http://dx.doi.org/10.3892/ijo.2012.1330>] [PMID: 22246399]

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